REMARKS

The obviousness type double patenting rejection were overcome by concurrent filing of the appropriate terminal disclaimers

The obviousness type double patenting rejection invoked issued copending application serial number 10/389071 and United States Patent No. 6,740,676. Terminal disclaimers regarding these two references are filed concurrently with the present response, thereby overcoming these grounds of rejection.

Rejection of the Claims pursuant to 35 U.S.C. section 102 was overcome by the present amendment

Claims 1 –9 and 28 – 32 were rejected as anticipated by U.S. Patent Application No. US 2004/0043044 (*Granger et al.*) This ground of the rejection was obviated by cancellation of Claims 1 – 9 and 28 – 32. In this regard it is noted that after this cancellation all remaining claims of the application, except for Claim 33 and 34, define the compounds having inhibitory effect on CP450RAI by chemical structure. The *Granger et al.* reference does not show these chemical structures.

Claim 33 is drawn to a compound which is an esther of retinol (a defined structure) with a compound having inhibitory effect on the enzyme CP450RAI. Again, the *Granger et al.* reference does not disclose this structure. Accordingly, the rejection for anticipation over this reference should be withdrawn in its entirety.

Regarding the rejection of claims pursuant to 35 U.S.C Section 112, second paragraph

Claims 17 – 23 were rejected because Claim 16 did not have the appropriate antecedent basis for the situation where the variable R_2 is hydrogen. This ground of the rejection has been overcome by inserting

"hydrogen" in the appropriate place. Similarly, "hydrogen" was also inserted into the definition of R_2 in Claim 10. The specification was also amended on pages 23 and 24 regarding Formula A and Formula B by inserting "hydrogen" into the definition of the variable R_2.

The foregoing amendments of the specification and of Claims 10 and 16 do NOT constitute new matter for several reasons.

Regarding Formula A, the third line from the bottom of page 23 states that "preferably "R_2 is H", and originally filed Claim 14 shows a compound where R_2 is in fact hydrogen.

Regarding Formula B, the fourth paragraph of page 25 states that in the preferred compound the aromatic portion of the chroman nucleus is substituted only by the variable **Y** in the 8 position and by the carbonyloxy-phenyl or ethynyl group in the 6 position. This means that in these preferred compounds R_2 is hydrogen. Moreover, page 27 of the specification shows a number of actual preferred compounds where the variable R_2 is indeed hydrogen, and originally filed Claims 18, 19 and 20 show the same thing.

Rejection of the claims for indefiniteness on the grounds that the terms "retinoid" and "a derivative of vitamin A having vitamin A like biological activity" are not adequately defined is respectfully traversed.

The term retinoid is well known and understood by those having ordinary skill in the art. This is amply demonstrated, for example, by a search of all United States patents issued since 1976 which have the term "retinoid" in their title. Applicant's undersigned attorney performed such a search on the U.S Patent Office' publicly available website and obtained 287 "records". A print-out demonstrating this search is enclosed as Exhibit 1. An article titled "Current Use and Future Potential Role of Retinoids in Dermatology" in the scientific publication "Drugs 1997 Mar. 53(3) 358 –

388" is enclosed here as Exhibit 2. The Examiner's attention is drawn to the definition of "retinoids" on page 359 of this review article where it is stated:

" 'Retinoids' is a generic term that includes both naturally occurring molecules and also synthetic compounds showing specific biological activities resembling those of vitamin A (retinol)."

The just quoted statement and the further reading of this article proves without any doubt that the term "retinoid" as well as the term "a derivative of vitamin A having vitamin A like biological activity" are well defined and well understood by persons having ordinary skill in the art.

Moreover, it is respectfully submitted that the rejection for the allegedly inadequate definition of the terms "retinoid" or of "a derivative of vitamin A having vitamin A like biological activity" is *a priori* inapplicable to each outstanding claim of the application where the compound of category (2) is defined simply as "Vitamin A". These claims are 11, 13, 15, 17, 20, and 23. Moreover, in Claim 33 the structure particularly shown is retinol so that the rejection for indefiniteness is cannot be applicable to this claim.

Still further, its is noted that Claims 15, 20, and 23 are drawn to a method using a combination of a single compound of defined structure with Vitamin A. Again, the rejection for indefiniteness *a priori* cannot be applicable to these claims.

<u>Rejection of the method claims for lack of enabling disclosure is in error and should not be maintained</u>

With regard to any possible or potential issue as to the adequate teaching of what is a "retinoid" or "a derivative of vitamin A having

vitamin A like biological activity" the remarks regarding 35 U.S.C section 112, second paragraph are also applicable here.

With regard to the Office Action stating that the teaching is inadequate because the claims are drawn to a method of treating "any" disease it is noted that the claims in issue do not mention any specific disease. They are drawn to inhibiting the enzyme CP450RAI by administering an inhibitory compound of defined chemical structure (category 1) and at the same time administering a retinoid or Vitamin A or a compound having Vitamin A like biological activity (category 2). That the compounds of category 1 inhibit the enzyme CP450RAI is adequately demonstrated in the present specification.

The law is well established that in order to evaluate patentability, assays, even in vitro assays, accepted in the state of the art are sufficient to provide an adequate disclosure provided the art considers the assay to be indicative of the ability or probability of the compounds to treat, ameliorate or prevent certain diseases and conditions. Thus, knowledge of the nature of "retinoids", knowledge and demonstrated ability of the compounds of this invention to inhibit the enzyme P450RAI which lessens the metabolic break down of retinoids in the body, are sufficient to enable the claims which call for inhibition of that enzyme without mentioning any specific disease but showing the structure of the specific inhibitor compounds. For the same reasons, methods using the *combination* of the compounds of the invention inhibiting the breakdown of "retinoids" with retinoids (and specifically with Vitamin A) are also enabled. A person of ordinary skill in the art the will be able to use, without undue experimentation, the methods of the invention in light of the present disclosure and knowledge of prior art.

In light of the foregoing, all outstanding claims of the present application are in *prima facie* allowable condition, and their early allowance is respectfully solicited.

In the event the Examiner is of the opinion that a telephone conference with the undersigned attorney would materially facilitate the final disposition of this case, she is respectfully requested to telephone the undersigned attorney at the below listed telephone number.

Respectfully submitted

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